Hematologic and Neoplastic Diseases

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393. Two weeks after a viral syndrome, a 2-year-old child develops bruising and generalized petechiae, more prominent over the legs. No hepatosplenomegaly or lymph node enlargement is noted. The examination is otherwise unremarkable. Laboratory testing shows the patient to have a normal hemoglobin, hematocrit, and white blood cell (WBC) count and differential. The platelet count is 15,000/μL. Which of the following is the most likely diagnosis?

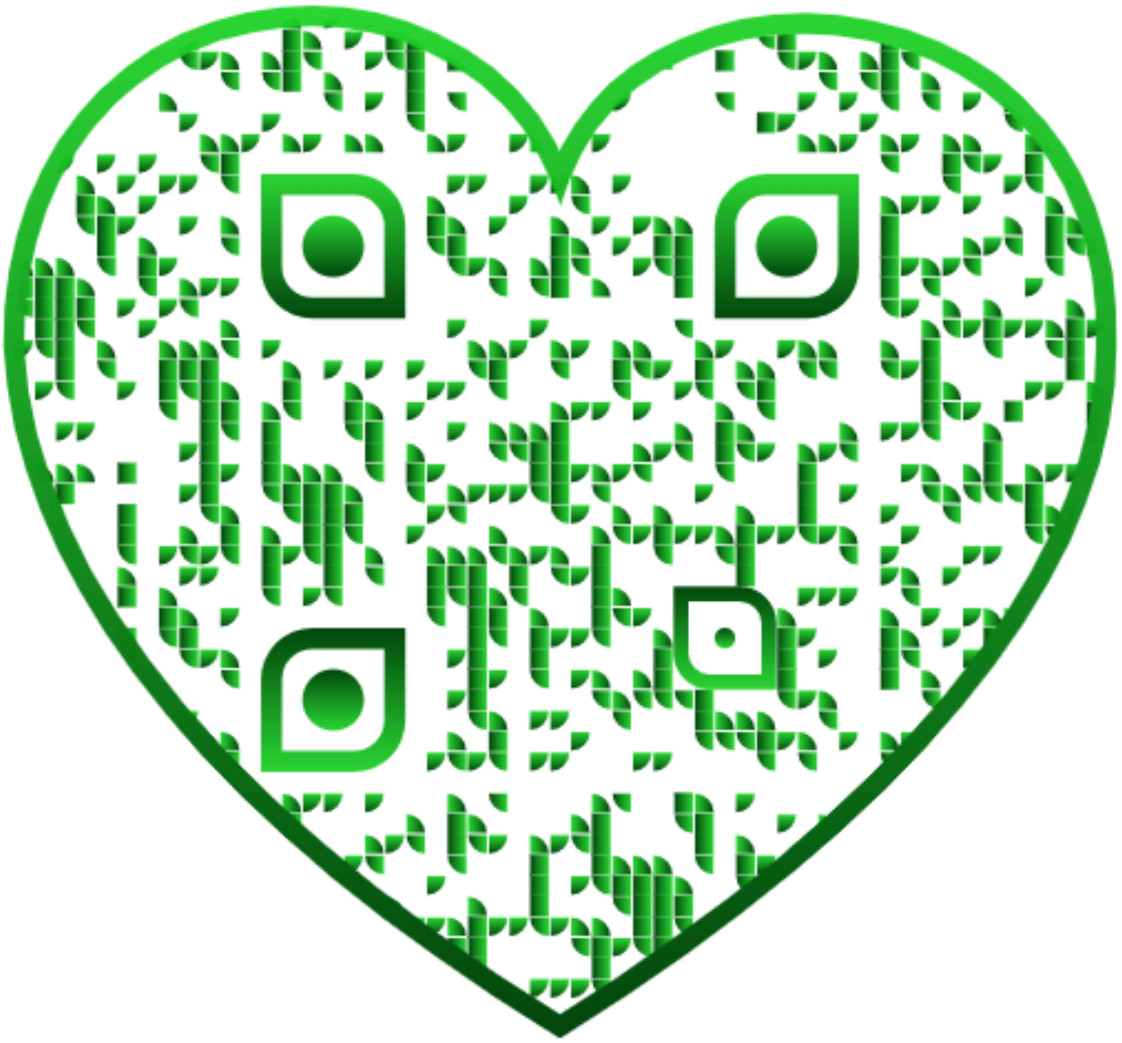
a. Von Willebrand disease (vWD)
b. Acute leukemia
c. Idiopathic (immune) thrombocytopenic purpura (ITP)
d. Aplastic anemia
e. Thrombotic thrombocytopenic purpura

394. An 11-month-old African American boy has a hematocrit of 24% on a screening laboratory done at his well-child checkup. Further testing demonstrates: hemoglobin 7.8 g/dL; hematocrit 22.9%; leukocyte count 12,200/μL with 39% neutrophils, 6% bands, 55% lymphocytes; hypochromia on smear; free erythrocyte protoporphyrin (FEP) 114 μg/dL; lead level 6 μg/dL whole blood; platelet count 175,000/μL; reticulocyte count 0.2%; sickle-cell preparation negative; stool guaiac-negative; and mean corpuscular volume (MCV) 64 fL. Which of the following is the most appropriate recommendation?

a. Blood transfusion
b. Oral ferrous sulfate
c. Intramuscular iron dextran
d. An iron-fortified cereal
e. Calcium EDTA

First Line

Response to a therapeutic trial of iron is an appropriate and cost-effective method of diagnosing iron-deficiency anemia



395. The parents of a previously healthy 2-year-old child note her to be pale and bring her to your clinic for evaluation. She currently has no fever, nausea, emesis, bone pain, or other complaints. Her examination is significant for pallor, tachycardia, and a systolic ejection murmur, but she has no organomegaly. Her complete blood count (CBC) reveals a hemoglobin of 4 g/dL, normal indices for age, a WBC count of 6.5/μL, and a platelet count of 750,000/μL. Her reticulocyte count is 0%. Coombs test is negative. Her peripheral blood smear shows no blast forms and no fragments. Red blood cell (RBC) adenosine deaminase levels are normal. A bone marrow reveals markedly decreased erythroid precursors. Which of the following is this child's likely diagnosis?

a. Diamond-Blackfan anemia
b. Sickle-cell anemia
c. Pearson marrow-pancreas syndrome
d. Iron deficiency anemia
e. Transient erythroblastopenia of childhood

the most common acquired RBC aplasia in children. This condition is commonly diagnosed between the ages of 1 to 3 years and some affected children have a history of a recent viral infection; (parvovirus B19 is usually specifically excluded)

396. On a routine-screening CBC, a 1-year-old is noted to have a microcytic anemia. A follow-up hemoglobin electrophoresis demonstrates an increased concentration of hemoglobin A2. The child is most likely to have which of the following?

a. Iron deficiency
b. β-Thalassemia trait Minor
c. Sickle-cell anemia
d. Chronic systemic illness
e. Lead poisoning

397. After being delivered following a benign gestation, a newborn infant is noted to have a platelet count of 35,000/μL, decreased fibrinogen, and elevated fibrin spilt products. On examination you note a large cutaneous hemangioma on the abdomen that is purple and firm. Which of the following anomalies might also be expected in this infant?

a. Kaposiform hemangioendothelioma
b. Nevus simplex
c. Nevus flammeus
d. PHACE(S) syndrome
e. Infantile fibrosarcoma

398. A 4-year-old previously well African American boy is brought to the office by his aunt. She reports that he developed pallor, dark urine, and jaundice over the past few days. He stays with her, has not traveled, and has not been exposed to a jaundiced person, but he is taking trimethoprim sulfamethoxazole for otitis media. The CBC in the office shows a low hemoglobin and hematocrit, while his "stat" serum electrolytes, blood urea nitrogen (BUN), and chemistries are remarkable only for an elevation of his bilirubin levels. His aunt seems to recall his 8-year-old brother having had an "allergic reaction" to aspirin, which also caused a short-lived period of anemia and jaundice. Which of the following is the most likely cause of this patient's symptoms?

a. Hepatitis B
b. Hepatitis A
c. Hemolytic-uremic syndrome
d. Gilbert syndrome
e. Glucose-6-phosphate dehydrogenase deficiency

399. Your sister who lives in another state sends via e-mail photographs of her 6-month-old infant. You note the child has a white reflection from one of his eyes. You hastily assist in arranging an urgent pediatric ophthalmologic evaluation. Your sister immediately accesses the Internet and begins to ask questions of you. Which of the following statements found by your sister is correct?

a. Most cases of retinoblastoma are unilateral and hereditary.
b. Cure rates for retinoblastoma treated in the United States exceed 90%.
c. Biopsy is usually performed to confirm the diagnosis.
d. Intraocular calcifications are an unusual finding and suggest worse prognosis.
e. Patients with the hereditary form of retinoblastoma are at significantly increased risk of leukemia in later years.

400. A 2950-g (6.5-lb) black baby boy is born at home at term. On arrival at the hospital, he appears pale, but the physical examination is otherwise normal. Laboratory studies reveal the following: mother's blood type A, Rh-positive; baby's blood type O, Rh-positive; hematocrit 38%; and reticulocyte count 5%. Which of the following is the most likely cause of the anemia?

a. Fetomaternal transfusion
b. ABO incompatibility
c. Physiologic anemia of the newborn
d. Sickle-cell anemia
e. Iron-deficiency anemia

401. A father brings his 3-year-old daughter to the emergency center after noting her to be pale and tired and with a subjective fever for several days. Her past history is significant for an upper respiratory infection 4 weeks prior, but she had been otherwise healthy. The father denies emesis or diarrhea, but does report his daughter has had leg pain over the previous week, waking her from sleep. He also reports that she has been bleeding from her gums after brushing her teeth. Examination reveals a listless pale child. She has diffuse lymphadenopathy with splenomegaly but no hepatomegaly. She has a few petechiae scattered across her face and abdomen and is mildly tender over her shins, but does not have associated erythema or joint swelling. A CBC reveals a leukocyte count of 8,000/μL with a hemoglobin of 4 g/dL and a platelet count of 7,000/μL. The automated differential reports an elevated number of atypical lymphocytes. Which of the following diagnostic studies is the most appropriate next step in the management of this child?

a. Epstein-Barr virus titers
b. Serum haptoglobin
c. Antiplatelet antibody assay
d. Reticulocyte count
e. Bone marrow biopsy

Children who present with symptoms that suggest leukemia

402. While bathing her newly-received 2-year-old son, a foster mother feels a mass in his abdomen. A thorough medical evaluation of the child reveals aniridia, hypospadias, horseshoe kidney, and hemihypertrophy. Which of the following is the most likely diagnosis for this child?

also in Turner synd.

a. Neuroblastoma
b. Wilms tumor
c. Hepatoblastoma
d. Rhabdomyosarcoma
e. Testicular cancer

403. A healthy 1-year-old child comes to your office for a routine checkup and for immunizations. His parents have no complaints or concerns. The next day, the CBC you performed as customary screening for anemia returns with the percentage of eosinophils on the differential to be 30%. Which of the following is the most likely explanation?

a. Bacterial infections
b. Chronic allergic rhinitis
c. Fungal infections
d. Helminth infestation
e. Tuberculosis

404. A 2-year-old child in shock has multiple nonblanching purple lesions of various sizes scattered about on the trunk and extremities; petechiae are noted, and oozing from the venipuncture site has been observed. The child's peripheral blood smear is shown below. Clotting studies are likely to show which of the following?

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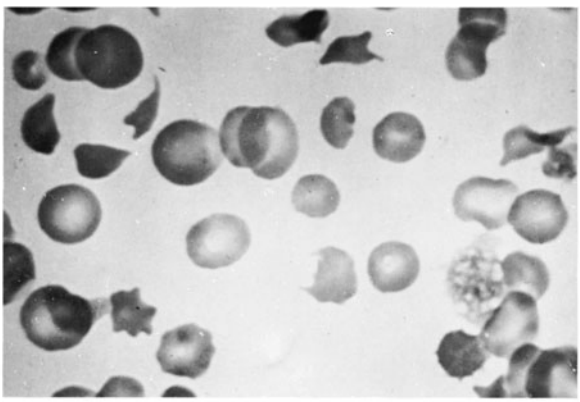


a. Increased levels of factor V and VIII
b. A decreased prothrombin level
c. An increased fibrinogen level
d. The presence of fibrin split products فایبرین متکسر
e. Normal partial thromboplastin time (PTT)

405. A male infant was found to be jaundiced 12 hours after birth. At 36 hours of age, his serum bilirubin was 18 mg/dL, hemoglobin concentration was 12.5 g/dL, and reticulocyte count 9%. Many nucleated RBCs and some spherocytes were seen in the peripheral blood smear. The differential diagnosis should include which of the following?

a. Pyruvate kinase deficiency
b. Hereditary spherocytosis early jaundice But Coombs ⊖
c. Sickle-cell anemia
d. Rh incompatibility
e. Polycythemia

406. On a routine well-child examination, a 1-year-old boy is noted to be pale. He is in the 75th percentile for weight and the 25th percentile for length. Results of physical examination are otherwise normal. His hematocrit is 24%. The answer to which of the following questions is most likely to be helpful in making a diagnosis?

a. What is the child's usual daily diet?
b. Did the child receive phototherapy for neonatal jaundice?
c. Has anyone in the family received a blood transfusion?
d. Is the child on any medications?
e. What is the pattern and appearance of his bowel movements?

407. A 10-year-old boy is admitted to the hospital because of bleeding. Pertinent laboratory findings include a platelet count of 50,000/μL, prothrombin time (PT) of 15 seconds (control 11.5 seconds), activated partial thromboplastin time (aPTT) of 51 seconds (control 36 seconds), thrombin time (TT) of 13.7 seconds (control 10.5 seconds), and factor VIII level of 14% (normal 38%-178%). Which of the following is the most likely cause of his bleeding?

a. Immune thrombocytopenic purpura (ITP)
b. Vitamin K deficiency
c. Disseminated intravascular coagulation (DIC) كلشي ناقص بالتحاليل
d. Hemophilia A
e. Hemophilia B

408. A 17-year-old adolescent comes to your office seeking help for "heavy" menses. Your review of systems also reveals weekly epistaxis. Her only significant past history includes a tonsillectomy at age 6 after which she required blood transfusion for excessive bleeding. Her family history includes several people who seem to bleed and bruise more easily than others. The patient's mother required a hysterectomy after child birth for excessive hemorrhage. You order a variety of laboratory tests. The patient has a hemoglobin of 6.5 mg/dL with an MCV of 60%; her platelet count is 350,000/μL. Her von Willebrand antigen and her von Willebrand factor (vWF) activity (ristocetin cofactor activity) are decreased. Her vWF is reported as normal but in decreased amounts. You have been unable to reach her to report the findings, but when she calls about 1 week later she reports she is having a mild to moderate nosebleed. You initiate therapy with which of the following?

a. Aminocaproic acid (Amicar)
b. vWF concentrate alone
c. vWF with factor VIII
d. Desmopressin (DDAVP)
e. Intravenous immunoglobulin (IVIG)

409. Over the previous 2 to 3 weeks, a very active 13-year-old white boy is noted by his family to have developed deep pains in his leg that awaken him from sleep. The family brings him to your office with a complaint of a swelling over his distal leg, which he attributes to his being kicked while playing soccer about 1 week ago. He has had no fever, headaches, weakness, bruising, or other symptoms. A radiograph of the leg is shown below. Which of the following is the most likely explanation for his pain?

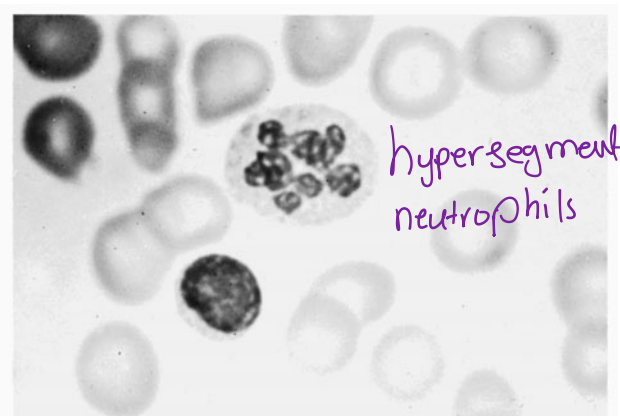
(Courtesy of Susan John, MD.)

a. Growing pains
b. Leukemia
c. Osteomyelitis
d. Bone fracture
e. Osteosarcoma

410. An otherwise healthy 17-year-old complains of swollen glands in his neck and groin for the past 6 months and an increasing cough over the previous 2 weeks. He also reports some fevers, especially at night, and possibly some weight loss. On examination, you notice that he has nontender cervical, supraclavicular, axillary, and inguinal nodes, no hepatosplenomegaly, and otherwise looks to be fairly healthy. Which of the following would be the appropriate next step?

a. Biopsy of a node
b. CBC and differential
c. Trial of antituberculosis drugs
d. Chest radiograph
e. Cat-scratch titers

411. An otherwise healthy child has on his 1-year-old routine CBC the polymorphonuclear neutrophil shown below. This child likely has which of the following?

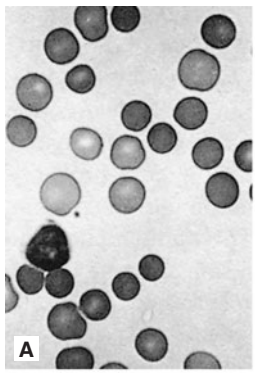


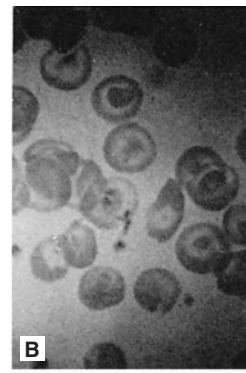
a. Malignancy
b. Iron deficiency
c. Folic acid deficiency
d. Döhle inclusion bodies
e. The Pelger-Huët nuclear anomaly

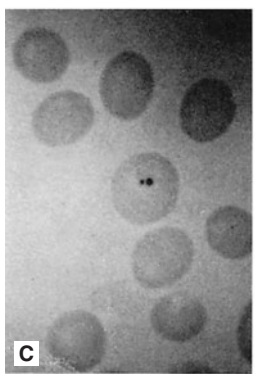
Questions 412 to 415

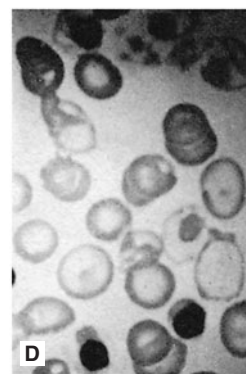
412-c, 413-d, 414-a, 415-b.

For each disorder listed below, select the peripheral blood smear with which it is most likely to be associated. Each lettered option may be used once, more than once, or not at all.









412. An 8-year-old patient with sickle-cell anemia

413. A 7-month-old boy with severe anemia requiring transfusions, heart failure, hepatosplenomegaly, and weakness

414. A 3-day-old newborn with anemia and pathologic hyperbilirubinemia requiring phototherapy

415. A completely asymptomatic, healthy 1-year-old whose routine CBC reveals an abnormality

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Hematologic and Neoplastic Diseases

Answers

393. The answer is c. *(Hay et al, pp 860-862. Kliegman et al, pp 2082-2084. McMillan et al, pp 1731-1733. Rudolph et al, pp 1556-1557.)* In children, ITP is the most common form of thrombocytopenic purpura. In most cases, a preceding viral infection can be noted. No diagnostic test identifies this disease; exclusion of the other diseases listed in the question is necessary. In this disease, the platelet count is frequently less than 20,000/μL, but other laboratory tests yield essentially normal results, including the bone marrow aspiration (if done). Complications are uncommon; significant bleeding occurs in only 5% of cases and intracranial hemorrhage is even rarer. The treatment of childhood ITP is controversial. Patients with mild symptoms such as bruising and self-limited epistaxis may be observed, while patients with significant bleeding should be treated. IVIG and corticosteroids are effective in causing a rapid increase in platelet count, but controversy exists surrounding the use of prednisone before ruling out leukemia with a bone marrow aspirate. For Rh-positive patients with a working spleen, the use of anti-D immunoglobulin also results in an increase in platelet count. For patients with chronic (> 1 year) ITP, a splenectomy may be helpful.

Aplastic anemia is unlikely if the other cell lines are normal. Von Willebrand disease might be expected to present with bleeding and not just bruising. It is unlikely that acute leukemia would present with thrombocytopenia only. Thrombotic thrombocytopenic purpura is rare in children.

394. The answer is b. *(Hay et al, pp 837-838. Kliegman et al, pp 2014-2017. McMillan et al, pp 1692-1694. Rudolph et al, pp 1525-1528.)* Response to a therapeutic trial of iron is an appropriate and cost-effective method of diagnosing iron-deficiency anemia. A prompt reticulocytosis and rise in hemoglobin and hematocrit follow the administration of an oral preparation of ferrous sulfate. Intramuscular iron dextran should be reserved for situations in which compliance cannot be achieved, since this treatment is expensive, painful, and no more effective than oral iron. Dietary modifications, such as

limiting the intake of cow's milk and including iron-fortified cereals along with a mixed diet, are appropriate long-term measures, but they will not make enough iron available to replenish iron stores. The gradual onset of iron-deficiency anemia enables a child to adapt to surprisingly low hemoglobin concentrations. Transfusion is rarely indicated unless a child becomes symptomatic or is further compromised by a superimposed infection.

When the iron available for production of hemoglobin is limited, free protoporphyrins accumulate in the blood. Levels of erythrocyte protoporphyrin (EP) are also elevated in lead poisoning. Iron-deficiency anemia can be differentiated from lead intoxication by measuring blood lead, which should be less than 10 μg/dL.

395. The answer is e. *(Hay et al, pp 836-837. Kliegman et al, pp 2006-2009. McMillan et al, pp 1707-1709 . Rudolph et al, pp 1566-1567.)* This child has transient erythroblastopenia of childhood (TEC), the most common acquired RBC aplasia in children. This condition is commonly diagnosed between the ages of 1 to 3 years and some affected children have a history of a recent viral infection; however, no specific virus has been implicated (parvovirus B19 is usually specifically excluded). Physical findings are minimal and include pallor and tachycardia. Laboratory studies reveal a profound anemia and reticulocytopenia with a marked reduction in erythrocyte precursors in the marrow. RBC adenosine deaminase (ADA) levels are normal. The condition lasts for several months, and may require 1 or 2 transfusions, but ultimately is self-limited. Steroids are not helpful.

Alternative diagnoses with this presentation include Diamond-Blackfan anemia (DBA), but this condition is congenital and usually presents in infancy; RBC ADA levels are usually elevated. In addition, about half of patients with DBA will have congenital anomalies including short stature, cranial abnormalities, and upper extremity abnormalities. Pearson marrow-pancreas is another form of congenital hypoplastic anemia, including poor growth, pancreatic fibrosis with insulin-dependant diabetes, and muscle and nerve involvement. Early death is typical. Sickle-cell patients usually have evidence of ongoing hemolysis on their smear, and iron deficiency causes a microscopic hypochromic anemia.

396. The answer is b. *(Hay et al, pp 844-845. Kliegman et al, pp 2033-2037. McMillan et al, pp 1699-1700. Rudolph et al, pp 1536-1538.)* The concentration of hemoglobin A2 is increased in β-thalassemia trait (also called β-thalassemia minor). Patients have a single abnormal gene for the β-globin component

of hemoglobin; they do not typically have problems aside from a mild microcytic anemia. It is important to distinguish between β-thalassemia trait and the more common iron deficiency anemia, as iron is not useful to patients with β-thalassemia trait. In severe iron deficiency, hemoglobin A2 may be decreased. In mild to moderate iron deficiency, the level of hemoglobin A2 is normal. The level is also normal in sickle-cell anemia, chronic systemic illness, and lead poisoning.

397. The answer is a. *(Hay et al, p 863. Kliegman et al, pp 2156-2157, 2488. McMillan et al, pp 1813-1814. Rudolph et al, pp 1203-1208.)* The child in the question likely has Kasabach-Merritt phenomenon, which is seen with large vascular anomalies (ie, kaposiform hemangioendothelioma and tufted angioma). Platelet and RBC sequestration within the vascular tumor causes peripheral thrombocytopenia, coagulopathy, and microangiopathic hemolytic anemia. Treatment options include corticosteroids, α-interferon, and vincristine. Surgery frequently results in excessive bleeding.

Nevus simplex is a common minor vascular malformation seen on the glabella, eyelids, and nape of the neck in newborns; such lesions on the face are also called "angel kiss," while lesions on the back of the neck are called "stork bite." Nevus flammeus, or port wine stain, is a large sharply demarcated pink to purple vascular malformation that can occur anywhere. Port wine stain involving the V1 distribution of the trigeminal nerve should raise the suspicion of Sturge-Weber syndrome. PHACE(S) syndrome includes **p**osterior fossa malformations, large facial **h**emangiomas, **a**rterial abnormalities, **c**oarctation of the aorta, **e**ye abnormalities, and **s**ternal defects. Infantile fibrosarcoma is a malignant congenital tumor that can be easily mistaken for an infantile hemangioma; a high index of suspicion is required to investigate further if a "hemangioma" is not resolving as expected.

398. The answer is e. *(Hay et al, pp 849-850. Kliegman et al, pp 2040-2042. McMillan et al, pp 2461-2462. Rudolph et al, pp 1542-1543.)* Synthesis of the RBC enzyme glucose-6-phosphate dehydrogenase (G6PD) is determined by genes on the X chromosome, and the pattern of inheritance is X-linked recessive. The enzyme found in most populations is termed G6PDB1. There are more than 380 deficient variants of the enzyme, affecting over 100 million people worldwide. Among them is variant G6PDA1, a mutant enzyme affecting about 13% of African American males and 2% of African American females. The disease occurs, though less commonly, in other ethnic groups, including Middle Eastern, African, and Asian groups. Deficiency of G6PD

compromises the generation of reduced glutathione and upon exposure to oxidant agents such as sulfa drugs, antimalarials, nitrofurans, naphthalene mothballs, or infection, a hemolytic episode usually occurs. The degree of hemolysis depends on the nature of the oxidant and severity of the enzyme deficiency. In African Americans, the older, more G6PD-deficient cells are destroyed, but since young cells have sufficient enzyme to prevent further RBC destruction even if the inciting factor is still present, the hemolytic crisis is usually self-limited. Blood transfusion may be unnecessary. In African Americans, premature testing for the enzyme immediately after a hemolytic episode can lead to a false-negative result, since the newly produced RBCs in the circulation have a higher G6PD enzyme activity. The older RBCs containing Heinz bodies (insoluble precipitates resulting from oxidation), the "bite cells" (RBCs after the removal of the Heinz bodies), and cell fragments are removed from the circulation within 3 to 4 days. In the severe Mediterranean type, young as well as old RBCs are enzyme deficient. Recovery is signaled by the appearance of reticulocytes and a rise in hemoglobin.

Hepatitis A or B will often occur after an exposure, and usually does not cause anemia as a presenting sign. Gilbert syndrome presents with episodes of jaundice, but not anemia. Hemolytic-uremic syndrome must be considered in a clinical situation similar to that presented, but the absence of uremia makes the diagnosis less likely.

399. The answer is b. *(Hay et al, pp 908-909. Kliegman et al, pp 2151-2152. McMillan et al, pp 1786-1788. Rudolph et al, pp 2395-2396.)* Retinoblastoma is an uncommon malignancy in children, with a worldwide incidence of 1 case per 18 to 30,000 live births with an equal male to female incidence. Diagnosis is usually made in the first or second year of life, typically during a routine physical examination or by parents noting a white reflection in a flash photograph. With early detection, more than 90% of cases can be cured, but vision is frequently lost in the affected eye. The most common presentation is a spontaneous unilateral tumor, accounting for 60% of cases. Hereditary tumors are less common, with a bilateral hereditary presentation accounting for 25% of cases, and unilateral hereditary tumor accounting for 15%. Biopsy is not indicated; diagnosis is made by typical findings on ophthalmologic examination, including a white or pink mass protruding from the retina into the vitreous matter, and intraocular calcifications. The genetic defect involved in the hereditary form also puts the patient at significantly elevated risk of soft tissue tumors years later, most commonly osteosarcoma (40%) but also including soft tissue sarcomas and malignant melanoma.

400. The answer is a. *(Hay et al, pp 59-60. Kliegman et al, pp 766-768. McMillan et al, pp 442-443. Rudolph et al, pp 197-199.)* The absence of a major blood group incompatibility and the finding of a normal reticulocyte count argue strongly in favor of a recent fetomaternal transfusion, probably at the time of delivery. A Kleihauer-Betke stain for fetal hemoglobin-containing RBCs in the mother's blood would confirm the diagnosis. After birth, erythropoiesis ceases, and the progressive decline in hemoglobin values, reaching a nadir at 6 to 8 weeks of age, has been termed physiologic anemia of infancy. Iron-deficiency anemia can be seen in the term infant between 9 and 24 months of age when the iron stores derived from circulating hemoglobin have been exhausted and an exogenous dietary source of iron has not been provided. The manifestations of sickle-cell disease do not appear until 4 to 6 months of life, coincident with the replacement of fetal hemoglobin with sickle hemoglobin.

401. The answer is e. *(Hay et al, pp 885-888. Kliegman et al, pp 2116-2120. McMillan et al, pp 1750-1758. Rudolph et al, pp 1594-1600.)* Children who present with symptoms that suggest leukemia with bone marrow failure require a bone marrow biopsy as soon as possible to clarify the diagnosis. Leukemias are the most common childhood malignancy, accounting for about 40% of all malignancies in children less than 15 years of age. Two thousand children a year are diagnosed with acute lymphoblastic leukemia (ALL) in the United States. Most are between the ages of 2 and 6 years; a male predominance is noted. All of the symptoms in the vignette are typically found with leukemia: clinical and laboratory evidence of marrow failure with anemia and thrombocytopenia. The WBC count can be normal, high, or low. Automated systems initially may report blast forms as atypical lymphocytes. A reticulocyte count would reflect lack of marrow response, but is nonspecific. EBV can cause fever and listlessness with lymphadenopathy, but is usually not associated with significant anemia and thrombocytopenia as described here. Haptoglobin may help distinguish hemolytic from nonhemolytic anemia, and an antiplatelet antibody would not explain the anemia.

402. The answer is b. *(Hay et al, pp 903-905. Kliegman et al, pp 2140-2143. McMillan et al, pp 1775-1777. Rudolph et al, pp 1614-1616.)* An abdominal mass is palpated in 85% of patients with Wilms tumor; abdominal pain is present in 40%, hypertension in about 60%, and hematuria in 12% to 24%. Because of the association of hemihypertrophy and aniridia with Wilms tumor, children with these findings should be followed with periodic physical examinations and abdominal sonograms, especially during their first 5 years. Wilms tumor and aniridia are associated with abnormalities on chromosome 11.

Neuroblastoma should also be considered in the differential diagnosis of abdominal mass, especially if fever, irritability, bone pain, limp, and diarrhea are present; in the case presented, however, the other features such as aniridia and horseshoe kidney make this diagnosis less likely than Wilms tumor.

403. The answer is d. *(Hay et al, p 859. Kliegman et al, pp 902-903. McMillan et al, pp 1716-1717. Rudolph et al, p 1555.)* Some common causes of eosinophilia in the peripheral blood smear include asthma, recurrent urticaria, infantile eczema, drug reactions, angioneurotic edema, helminth infections, collagen vascular disease, and some neoplasms. Allergic rhinitis can cause eosinophilia in nasal secretions, but usually does not cause dramatic peripheral eosinophilia.

404. The answer is d. *(Hay et al, pp 868-869. Kliegman et al, pp 2080-2081. McMillan et al, pp 1745-1746. Rudolph et al, p 1575.)* The clinical history and blood smear findings (fragmented cells and few platelets) presented in the question are typical of disseminated intravascular coagulation. The disorder, which can be triggered by endotoxin shock, results ultimately in the initiation of the intrinsic clotting mechanism and the generation of thrombin (prolonged PT and PTT, decreased fibrinogen concentration, and an increase in fibrin split products). Fibrin deposited in the microcirculatory system can lead to tissue ischemia and necrosis, further capillary damage, release of thromboplastic substances, and increased thrombin generation. Simultaneous activation of the fibrinolytic system produces increased amounts of fibrin split products, which inhibit thrombin activity. Of utmost importance in the treatment of children who have disseminated intravascular coagulation is the management of the condition that precipitated the disorder.

405. The answer is b. *(Hay et al, pp 840-841. Kliegman et al, pp 2020-2023. McMillan et al, pp 1701-1703. Rudolph et al, pp 1539-1540.)* The patient in the question has a hemolytic anemia and spherocytes on the smear. An increased number of spherocytes on peripheral smear can be seen in such conditions as hyperthermia, hereditary spherocytosis, G6PD deficiency, or ABO incompatibility (but usually not Rh incompatibility). Neonatal hyperbilirubinemia can be seen in patients with hereditary spherocytosis. The hemolytic manifestations of ABO incompatibility and hereditary spherocytosis are very similar. The blood types of the mother and of the infant should be determined along with the results of a direct Coombs test on the infant and the presence or absence of a family history of hemolytic disease (spherocytosis).

Sickle-cell disease would not be expected to cause problems in newborns because of protection by fetal hemoglobin. Hyperbilirubinemia can

be caused by polycythemia, but the spherocytes would be unusual, and the patient in the question had anemia for a newborn. Pyruvate kinase deficiency can cause neonatal hemolytic anemia, but spherocytes are not commonly seen.

406. The answer is a. *(Hay et al, pp 837-838. Kliegman et al, pp 2014-2017. McMillan et al, pp 1692-1694. Rudolph et al, pp 1525-1528.)* Iron-deficiency anemia is the most common nutritional deficiency in children between 9 and 15 months of age. Low availability of dietary iron, impaired absorption of iron related to frequent infections, high requirements for iron for growth, and, occasionally, blood losses, favor the development of iron deficiency in infants. A history regarding anemia in the family, blood loss, and gestational age and weight can help to establish the cause of an anemia. The strong likelihood is that anemia in a 1-year-old child is nutritional in origin, and its cause will be suggested by a detailed nutritional history.

407. The answer is c. *(Hay et al, pp 868-869. Kliegman et al, pp 2080-2081. McMillan et al, pp 1745-1746. Rudolph et al, p 1575.)* In disseminated intravascular coagulation (DIC), there is consumption of fibrinogen; factors II, V, and VIII; and platelets. Therefore, there is prolongation of PT, aPTT, and TT and a decrease in factor VIII level and platelet count. In addition, the titer of fibrin split production is usually increased. D-dimer is a fibrin breakdown product and may also be elevated in DIC.

The prolongation of PT, aPTT, and TT excludes the diagnosis of ITP. PT tests principally for factors I, II, V, VII, and X and is not prolonged in hemophilia A (factor VIII deficiency) or hemophilia B (factor IX deficiency). In vitamin K deficiency, there is a decrease in the production of factors II, VII, IX, and X, and PT and aPTT are prolonged. The thrombin time, which tests for conversion of fibrinogen to fibrin, however, should be normal, and the platelet count should also be normal.

408. The answer is d. *(Hay et al, p 868. Kliegman et al, pp 2071-2074. McMillan et al, pp 1740-1742. Rudolph et al, p 1573.)* Von Willebrand disease is the most common heritable bleeding disorder, with some studies suggesting prevalence of 1% to 2% in the general population. vWF participates in clot formation by adhering to areas of vascular damage and causing platelets to attach and activate. About 85% of cases of vWD are type I, resulting from decreased production of normal vWF. Several variants of type II vWD are described, with abnormal or dysfunctional vWF the etiology. Patients with type III, the most rare, have undetectable levels of vWF. In type I, desmopressin

alone can transiently increase the levels of vWF three- to fivefold, so it is frequently used for acute bleeding episodes.

Aminocaproic acid interferes with fibrinolysis and stabilizes a clot (once it is already formed) by inhibiting plasmin, but does not replace desmopressin in treating patients with VWD. vWF and vWF with factor VIII, are used in other types of vWD, but are not usually used first in type I for mild to moderate bleeding. IVIG is not used in vWD.

409. The answer is e. *(Hay et al, pp 797-799, 885-888, 905-906. Kliegman et al, pp 996, 2116-2122, 2147-2148, 2841-2845. McMillan et al, pp 1750-1758, 2497-2499. Rudolph et al, pp 858-859, 904-907, 1594-1604, 1610-1611, 2450-2451.)* The patient in the question likely has osteosarcoma, and the radiograph shows the expected "sunburst" pattern of bone formation. Osteosarcoma occurs most commonly in the second decade of life, and a bit more commonly in boys than in girls. It occurs in all ethnic groups (in contrast, Ewing sarcoma, another bone malignancy, rarely occurs in blacks). The lesion of osteosarcoma is found in the metaphyses of long bones, and usually presents with local pain and swelling. Predisposing factors include a history of retinoblastoma, Li-Fraumeni syndrome, Paget disease, or radiotherapy. Any bone or joint "injury" not responding with conservative therapy within a short period of time should be evaluated.

"Growing pains" are commonly seen in the school-age child. They present with deep, aching pain, usually in the muscles of the leg. They are most common in the evening, gone by the morning, and do not cause joint swelling, redness, heat, or systemic signs or symptoms. The etiology is unknown, but, despite the name, it is not related to growing. Leukemia can present with deep bone pain, but often other signs and symptoms, such as bruising, adenopathy, hepatosplenomegaly, fever, and pallor, will also be seen. Osteomyelitis can present as a localized pain, but systemic signs (such as fever) would also be expected. The radiograph of osteomyelitis would eventually demonstrate a more lytic lesion. Bone fractures can occur in the active child, but the presentation might include a better history of trauma, and the radiograph would demonstrate a fracture or callus formation rather than a sunburst pattern of bone growth.

410. The answer is d. *(Hay et al, pp 896-898. Kliegman et al, pp 2123-2126. McMillan et al, pp 1767-1768. Rudolph et al, pp 1607-1610.)* The patient in this question, especially with the pulmonary findings, may have Hodgkin disease. In underdeveloped countries, the peak incidence of Hodgkin disease

is in children under 10 years of age; however, in developed countries, the peak incidence occurs in late adolescence and young adulthood. Systemic symptoms of Hodgkin disease include fever, night sweats, malaise, weight loss, and pruritus. Although a biopsy of the node may prove to be necessary at some point, the first step would involve a radiograph, which may show mediastinal mass suspicious for Hodgkin disease. Depending on the results of the radiograph, a biopsy of a node may be indicated, especially if the question of Hodgkin (or other malignancy) remained high.

A tuberculosis skin test may be indicated, but a trial of antituberculosis drugs without a chest radiograph, a positive purified protein derivative (PPD), or other diagnostic evaluation indicating tuberculosis would be unwise. In Hodgkin disease, the CBC is not diagnostic, but may show nonspecific findings of anemia, neutropenia, or thrombocytopenia; they are useful in the staging process after the diagnosis has been confirmed by biopsy. The presenting complaint with multiple groups of swollen nodes is unlikely to be related to cat-scratch disease.

411. The answer is c. *(Hay et al, pp 838-839. Kliegman et al, pp 2011-2013. McMillan et al, pp 1694-1695. Rudolph et al, pp 1529-1530.)* The finding of hypersegmented neutrophils in the peripheral blood is one of the most useful laboratory aids in making an early diagnosis of folate deficiency. Serum folate levels become low in weeks with an inadequate dietary source. The Pelger-Huët anomaly is an inherited disorder in which neutrophils have no more than two lobes. Neutrophils in severe bacterial infections have toxic granulation, Döhle inclusion bodies, and cytoplasmic vacuoles.

412 to 415. The answers are 412-c, 413-d, 414-a, 415-b. *(Hay et al, pp 840-844, 848, 874. Kliegman et al, pp 2004, 2020-2023, 2032-2037, 2090. McMillan et al, pp 1698, 1699-1703, 2442. Rudolph et al, pp 1531-1534, 1536-1540, 1561.)* Howell-Jolly bodies (slide C) are small, spherical, nuclear remnants seen in the reticulocytes and, rarely, erythrocytes of persons who have no spleen (because of congenital asplenia or splenectomy) or who have a poorly functioning spleen (eg, in hyposplenism associated with sickle-cell disease). Ultrafiltration of blood is a unique function of the spleen that cannot be assumed by other reticuloendothelial organs.

A target cell is an erythrocyte with a membrane that is too large for its hemoglobin content; a thin rim of hemoglobin at the cell's periphery and a small disk in the center give the cell a target-like appearance. Target cells, which are more resistant to osmotic fragility than are other erythrocytes, are

seen in children who have α-thalassemia, hemoglobin C disease, or liver disease (eg, obstructive jaundice or cirrhosis). Thalassemia major (slide D) presents in the second 6 months of life with severe anemia requiring transfusion, heart failure, hepatosplenomegaly, and weakness. Later, the typical facial deformities (maxillary hyperplasia and malocclusion) can be seen in a patient inadequately transfused. The diagnosis can be made on peripheral blood smear by the presence of poorly hemoglobinized normoblasts in addition to target cells in the peripheral blood.

Uniformly small microspherocyte (less than 6 μm in diameter) are typical of hereditary spherocytosis (slide A). Because of a decreased surface to volume ratio, these osmotically fragile RBCs have an increased density of hemoglobin. Although spherical RBCs also can appear in other hemolytic states (eg, immune hemolytic anemia, microangiography, ABO incompatibility, and hypersplenism), their cellular volume is only irregularly augmented. Patients with hereditary spherocytosis can present in the newborn period with anemia, hyperbilirubinemia, and reticulocytosis. They may remain asymptomatic until adulthood, when they develop symptoms. After infancy, hepatosplenomegaly and gallstones are common.

Although hemoglobin C disease (slide B) is frequently a mild disorder, target cells constitute a far greater percentage of total RBCs than in thalassemia major. In the heterozygous state, no anemia or disease is noted, but target cells are seen. In the homozygous state, a moderately severe hemolytic anemia, reticulocytosis, and splenomegaly are seen, along with a smear containing a large number of target cells.

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